VOL. XIII. August, 1888. No. 8

THE

Journal

OF

Nervous and Mental Disease.

Original Articles.

A CONTRIBUTION TO THE PATHOLOGY OF TROPHIC DISORDERS OF THE MUSCULAR SYSTEM.*

By DAVID INGLIS, M.D.,

PROFESSOR OF NERVOUS AND MENTAL DISEASES IN THE DETROIT COLLEGE OF MEDICINE.

THE patients whom you have just seen present the following history:

Their grandparents lived to old age and, as far as can be learned, both were healthy themselves, and had brothers and sisters of excellent physique. They had a family consisting of one son and four daughters. This son, who died of accidental injury at the age of 45, was healthy and left a family of thirteen children, all healthy. The four daughters are themselves in good health, are all married and have families of boys and girls. The family of one daughter has as yet shown none of the hereditary tendencies now to be related. Of the remaining daughters, one, Eliza, now living in England, has been twice married and has had four sons and ten daughters; her daughters are healthy, but her oldest son from his earliest infancy showed marked muscular atrophy; he has however grown up and married, but is, at the present time, an entirely helpless cripple from the gradual increase of the disease. A younger son by her second husband has also been affected, and is now helpless; he is said to be apparently very muscular.

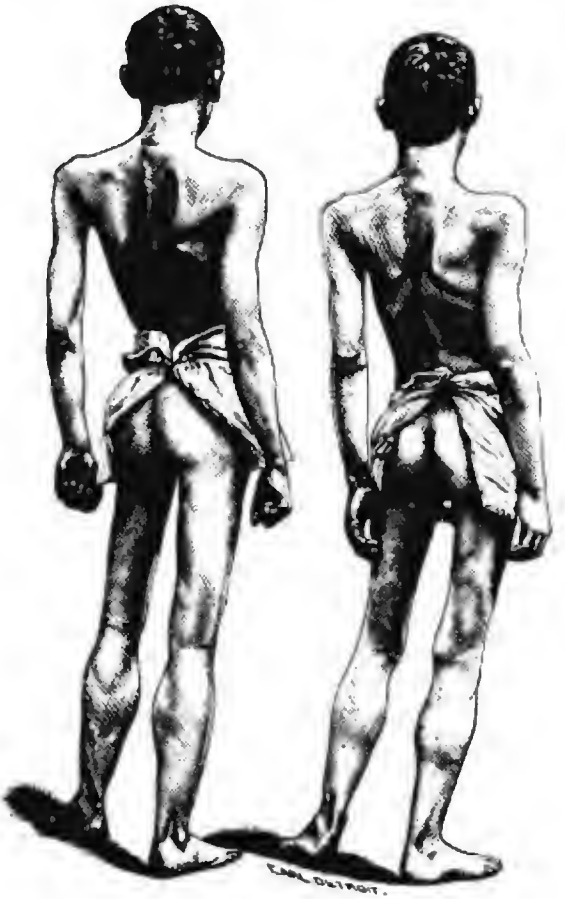
Of Eliza's daughters several are married; the eldest daughter has a son who is similarly affected.

* Read before the Detroit Medical and Library Association.

The next sister of Eliza, Mrs. K., has a family of four sons and one daughter, the latter healthy; of the sons, Herbert, the oldest, now aged 20 years, showed, from the time he began to walk, the first evidences of his disease. The parents noticed that the muscles of his arms instead of increasing seemed rather to grow smaller. When he had learned to walk, the attitude was with the shoulders held well back, and the shoulder blades were unusually prominent. Close questioning reveals no history either in this or in the two following of any sudden paralysis or other evidence of attacks of poliomyelitis anterior. The lad learned to walk at about the usual age, grew at the usual rate, and is now a tall young fellow. It is to be remarked that coincidently with the fact of extensive muscular atrophy there has taken place a certain amount of natural muscular growth. There is no defect in the bony development; and the muscles of the arms, while they have been atrophied since infancy, have yet grown both in length and size. The patient now presents the characteristic attitude which you have seen; his shoulders are thrown far back when standing, the spine curved with the convexity forward, the feet spread apart, one always in advance of the other, and one heel always off the ground. He rises from the sitting position by lifting as much of his weight as possible by the arms braced upon his knees; then, with feet widely extended and an extraordinary curving of the spine, he alternately braces his hands further and further up his thighs, and so climbs up his thighs. From lying on the floor, the process of standing is attained with difficulty, and in a similar manner. He first gets on his feet, legs extended on the thighs; then, from resting on feet and hands, goes through the same process of climbing.

Physical examination shows very extensive muscular atrophy, symmetrical in its distribution. The erector muscles of the back are most involved; those of the hand, forearm, arm, and shoulder are all involved; in grasping firmly, the pronators act to excess. The muscles of the buttocks and thighs are perhaps as well developed as could be expected, and the calves are developed out of all proportion.

They stand out rounded and hard, but the appearance of strength is fallacious; the muscles are nearly as hard and firm when at ease as when in contraction, and offer but feeble resistance.



HERBERT. FRED.

Owing to relative shortening, the feet are habitually in a position of slight talipes equinus, thus preventing his standing with both heels touching the floor. The picture, then, is complete of pseudohypertrophy of the muscles of the legs, with general muscular atrophy of the muscles of the back and upper extremities. Before leaving this case, I should

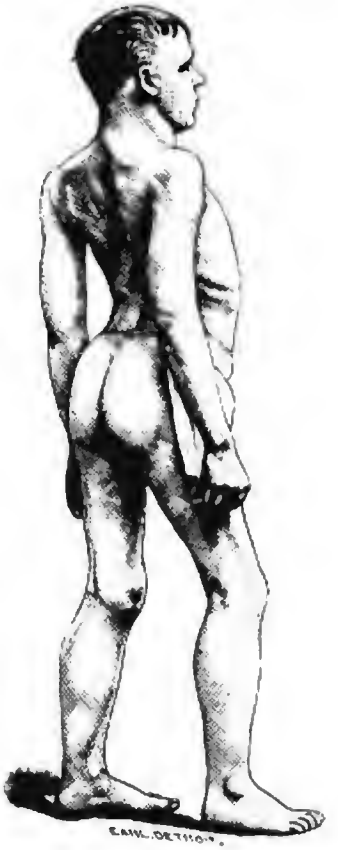
state that the boy's general health has been good; he has had no symptoms indicating any disorders of sensation or of voluntary motion save the weakness clearly caused by the state of the muscles themselves; his intelligence is good. Tendon reflexes absent.

The next brother, Fred, now aged 18, presents, as you see, as nearly as possible, the same appearance, the same gait and attitude, the same distribution of atrophied muscles, the same pseudohypertrophy of the calves. It would be impossible to more closely duplicate the entire group of symptoms, both as regards their character and extent; yet the history of the case presents this curious feature that in the case of Fred the *atrophic* changes have all taken place since the age of twelve years.

I am inclined to believe that the pseudohypertrophy was going on for a long period before that, for the boy states that he was always easily knocked down, but he was considered by his parents perfectly sound up to the age of twelve. He was vigorous and active as any young lad and with the full use of his arms and hands. Without any apparent illness, there gradually came on a weakness and wasting of the hands, arms and back. The order in which the muscles were affected, as far as can be learned, was first those of the back, then the forearm, the flexors of the arm, and last the shoulder muscles. It would be possible to claim that, in the elder brother, the apparent atrophy is simply the result of lack of development, but in this case the process has been one of distinct atrophy, ending in an identical condition; here, too, the tendon reflexes are absent.

Turning now to the third married sister, Mrs. King, we find that she has three sons and four daughters; her daughters are robust and healthy. Of her sons, George, now aged 19 years, is here present, and presents an appearance even more striking than the other two. His height is 5 feet $4\frac{1}{2}$ inches; his weight 130 pounds; but the first impression of him is that of an extraordinarily muscular young fellow. On physical examination we find an enormous pseudohypertrophy of the calves, buttocks, arms and forearms—

symmetrical; the erectors of the spine, on the contrary, are atrophied. The tendon reflexes and electrical reactions are the same as in his two cousins. Strikingly different as is his appearance the net result is the same. The same gait and attitude, the same method of attaining the erect position, the same muscular weakness. The history of this case



GEORGE.

also dates back to early infancy. A fat baby, he was supposed to be slow in learning to walk from his weight. When he did walk the gait was peculiar and unsteady. Hypertrophy of the calves was followed by that of the buttocks, then the triceps, and lastly the forearms.

Some ten years ago this lad developed a bronchocele.

which disappeared under treatment, but began to return two years ago and has now reached a large size, bilateral and soft. The oldest brother of George I also present, showing the malformation of his foot. He is a hard-working young man, aged 28, with no history of pseudo-hypertrophy or atrophy save that the deformity is the result of a stroke of paralysis occurring when he was about about a year old. His mother states that he could walk well at the early age of ten months, but shortly after was noticed to lie wherever he was put. By degrees it was noticed that he had lost the use of his right leg entirely, from the hip down. Later the control returned, and at seventeen months he began to walk again. Recognizing the difficulty of making a positive diagnosis at this late date, it yet seems fair to believe that this insidious paralysis of the leg, evidently of rapid onset followed by recovery of control in the main, but also by contracture and permanent deformity, was an attack of poliomyelitis anterior.

In none of the cases fibrillary twitching or paræsthesiæ were manifested.

Having thus presented the patient with this interesting family history, several questions present themselves. Notably the extraordinary uniformity of hereditary transmission through the female line to the male children. I am in correspondence with the members of the family in England, and hope soon to be able to elicit information upon other points, *e. g.*, whether the married cripple has children, and if so, what hereditary peculiarities may have occurred. It is interesting to note the fact that the mother, Eliza, being twice married, has children by both husbands, presenting the same inherited tendencies. The disease has now begun to show itself in the children's children, and the mysterious question awaits solution: what was the cause of the fatal gift of the mother to her daughters, and wherein lies the cause that only the daughters should transmit the inheritance which could only develop itself in the sons. It is evident that the explanation so frequently given of greater frequency of certain diseases in males, to wit, greater exposure to hardships, does not here apply. An interesting

series of cases of hereditary hæmophilia, showing an almost identical order of transmission, and involving five generations, is reported in the *London Lancet* of November, 1886.

Leaving the question of heredity, the problem at once presents itself: What is the bond of union between these varied cases—infantile atrophy, pseudohypertrophic paralysis, progressive muscular atrophy and bronchocele? The question has additional interest from the fact that there is at present a strong tendency to separate pseudohypertrophy from the atrophies of spinal origin, and to regard it as a purely muscular affection. Such a series of cases as that now presented seems to me to possess a distinct value in the elucidation of this question, which is one of vital importance if we ever hope to solve the problem of the successful treatment of these intractable cases.

The group embracing infantile atrophy, progressive muscular atrophy and pseudohypertrophic paralysis possess one common factor. Various as their symptoms, they are all affections of the motor apparatus, involving sooner or later the atrophy of groups of muscles with consequent loss of function. Before entering upon the bearing of this series of cases, let us recall the facts which have been established concerning the pathological changes in these affections. Beginning with infantile paralysis: The frequency of the occurrence of poliomyelitis anterior has enabled us to obtain very conclusive proof that the disease is distinctly an acute process by which a rapid atrophy of the multipolar cells of the anterior cornua is induced, which is accompanied by an immediate loss of function and followed by atrophy of certain groups of muscles. The acuteness of onset, the sudden comparatively widespread paralysis, the fact that the atrophy does not involve all of the muscles first paralyzed, and the fact that the atrophy follows the paralysis at a comparatively late date, proves to demonstration that the atrophic change has its starting point in the cord, that the muscular degeneration is secondary. While the atrophied muscles present a constant pathological appearance, the gray matter of the cord presents just as constant evidences of morbid process.

In progressive muscular atrophy the pathology is not disposed of so summarily. The course of the disease being slow it becomes difficult to state which post-mortem appearances are primary and which secondary.

All authors are agreed that the atrophied muscles give evidence of a chronic interstitial change, ordinarily termed a myositis. It is indeed questionable whether the process deserves to be thus considered as in any way inflammatory, being rather a substitution of a less highly organized tissue, but at any rate the process ends in a cirrhosis—muscle fibre disappears, connective tissue remains. The question hinges upon the lesions of the nerves and cord. A large number of observations have been made in which lesions of the sympathetic and of the spinal roots, as well as of the antero-lateral columns, have occasionally been noted, but the preponderance of evidence is clearly that the anterior cornua are in the greater number of cases the seat of degenerative changes. Ross believes that the diseased process begins in the gray matter about the central canal and spreads especially toward the anterior cornua and also perpendicularly, a theory which plausibly explains the erratic manner in which groups of muscles are involved as well as occasional sensory disturbances. The atrophy of the cells of the anterior cornua in greater or less number is the common, but it is to be borne in mind that, leaving out of account observations made many years ago, at a time when methods of examination were imperfect, there still remain cases in which observers of recognized ability have found the cord intact. Such cases demand consideration in formulating a theory of the disease.

The pathology of pseudohypertrophic paralysis presents still greater difficulty. The remarkable gross appearance of the muscular masses very naturally attracts attention. Frequent examination has shown that the process is, in this case as in the last, one of substitution. The normal connective tissue of the muscular substance is enormously increased, and amid the mass of connective tissue the muscular elements waste away and at last disappear. In the newly formed connective tissue occurs a more or less marked for-

mation of fatty tissue. These newer and more lowly organized tissues give the bulk to the muscle, but the atrophy of the true muscular substance is the same as in the progressive muscular atrophy. At a later period the adipose tissue, and even a considerable part of the connective tissue, may in time waste away, leaving the gross appearance, as well as the microscopical, indistinguishable from that resulting from progressive muscular atrophy. The pathological changes in the nervous apparatus have been examined in a much smaller number of cases than those of progressive muscular atrophy, and vary widely. In the greater number of cases lesions of the cord have been observed; but while in some atrophy of the anterior cornua has been present, in several the lesion has consisted in changes in the form and place of the central canal, while in others the cord has seemed intact.

The problem to be solved is, What is the relation between the changes in the muscle and those in the cord? Are we, with our present knowledge, justified in believing that progressive muscular atrophy is due to a primary lesion of the gray matter of the cord, to which the muscle changes are secondary? and, if so, on what ground are we to separate pseudohypertrophy from it, and consider the muscular change primary, those in the cord as non-essential?

I hold that, at whatever conclusion we arrive, the two diseases should be classed together. Clearly pseudohypertrophic paralysis is allied in the most intimate manner with lesions undoubtedly spinal; for, in cases of infantile paralysis, instead of the usual process of simple atrophy, this same pseudohypertrophy at times occurs.

It is evident, then, that an atrophic lesion in the cord can cause just that form of muscular change which does occur in pseudohypertrophied paralysis. This same process of lifomatosis also occurs in the progressive muscular atrophy of adults.

In order to throw some further light upon the enigma thus presented, it will be well to recall the pathological changes which occur in certain atrophic disorders due to toxic agents. In the case of alcoholic paraplegia, the symp-

toms are those of combined ataxia and progressive muscular atrophy, both of which groups may reach an extreme grade, so that the atrophy may be as complete as in a far advanced case of progressive muscular atrophy. When we seek for the seat of the pathological changes thus developed, we find the brunt of the affection has fallen upon the *conducting* nerves; while the muscle shows the usual atrophic changes, the nerves show evidences of widespread neuritis; but the cord in this case also seems to be intact.

In lead paralysis, likewise, the pathological changes seem usually to prove the existence of a neuritis; the atrophic muscular changes are present.

We have before us the enigma of atrophy of the muscle (varied in some cases by an apparent but fictitious hypertrophy, which does not alter the fact of a real atrophy). The atrophy is constant, and the connected nervous lesions have an inconstant location. Yet inconstant as are the lesions they still have this in common; they are all to be found either in the cells of the anterior cornua, in the course of the axis cylinders or in the muscular elements.

We speak of these as dissimilar elements, as if the cell were one thing, the nerve fibres another, and the muscle something quite different. A moment's reflection is sufficient to recall that from the ganglionic cell its protoplasm is continued by its axis cylinder process to the axis cylinder, and this, always unbroken, to the motor end plate, from which there seems to be a direct communication with the nuclei of the muscular elements; in other words, ganglionic cell, axis cylinder, and motor end plate are not three things, but one continuous mass of protoplasm.

Granting that excitory impulses travel uniformly over this route from central cell to muscular fibre, there yet remains the fact that the nutritive condition of this contiuous mass of protoplasm tends to uniformity. We have undoubted evidence of this in the well-known fact of descending degeneration. Once the axis cylinder is cut off from its connection with the motor cell, it dies; and it is the disconnected part which dies. Evidently the central point for the regulation of the life of the string is at the

gray cell; but the problem is not so simple. Granting that the cutting of the communications causes the death of the distal fragment by no means proves that while the communication remains a change in the nutritive condition of the distal extremity may not continuously influence the condition of the central end. If, then, the lesion in infantile paralysis be such as to immediately destroy the gray cells, we can conceive of the entire mass of protoplasm dying downwards. The cell being destroyed, the process is rapid; the disease has struck at the nutritive centre of the protoplasmic system. In multiple neuritis the break occurs lower down, but the degenerative process goes on to exert its influence on the muscular fibre. In progressive muscular atrophy it is still questionable whether the atrophy of the motor cells is primary or secondary, but in pseudohypertrophic muscular paralysis there would seem to be much reason to believe that the process makes its first appear- in the muscular substance. I submit that in diseases as slow in their progress as pseudohypertrophy and progressive muscular atrophy, it is reasonable to conceive that a process of degeneration slowly going on in the motor end plates might well influence the nutrition of the long-drawn-out strand of protoplasm of which the motor end plate is merely one portion. That such an origin for the degenerative process explains better than any other the anomaly of constant atrophic changes occurring in connection with nerve lesions of such varied location. We have not yet touched upon another question, viz., the increase of connective tissue and fatty deposit. To enter upon the consideration of this in detail would lead too far for our limits. Suffice that this fibrosis seems to be the customary endeavor of the organism to repair damages, that the irritative processes which lead to the atrophy of the muscular and nerve structures according to common experience might well be expected to cause an increase of the more lowly organized connective tissue.

The value of the series of cases presented lies in this, that they give evidence that the same inherited defect is shown to give rise in one case to an attack of poliomyelitis

anterior in several others of the family to either extraordinary muscular atrophy or extreme pseudohypertrophy. I have endeavored in this paper to show that the three diseases ought to be grouped together; the inherited defect groups them together, as we see here to-night. The common inheritance of these young men has been a tendency to degeneration of those protoplasmic strands which begin as motor cells and end as motor end plates or muscle nuclei.

To sum up, I would claim that muscular dystrophies can be properly divided into two classes: first, those in which a true paralysis occurs, in which there is a break in the motor conduction, under which are to be included acute and chronic myelitis anterior, amyotrophic lateral sclerosis, primary or secondary, and atrophies, due to neuritis or section of nerves; and a second class, in which no true paralysis exists, but an impairment of function proportionate to and dependent upon the muscular atrophy—in this class are progressive muscular atrophy and pseudohypertrophic paralysis.

I would also claim that there is a distinction to be made between the relation of the central and distal ends of a nerve fibre in the case of an entire severance of connection, and in the other case of maintenance of continuity with slow changes of the nutritive condition.

I would claim that both progressive muscular atrophy and pseudohypertrophy are essentially of spinal origin; that the cases in which the post-mortem examination shows the cord visibly intact do not invalidate this idea, but that the defect in the distal ends of the motor fibres, while not in every case accompanied by atrophy of the central cells, is yet the indication of an impaired activity of those cells.

The not unfrequent occurrence, in connection with pseudohypertrophy, of bronchocele, and, in other cases, of forms of mental disturbance, cannot be explained by a primary muscular disease, but admit of explanation as due to lesions of the sympathetic ganglia propagated from the cord.